International Journal of Mathematics and Statistics Studies
Vol.4, No.1, pp.30-49, February 2016
Published by European Centre for Research Training and Development UK (www.eajournals.org)

SENSITIVITY ANALYSIS OF LASSA FEVER MODEL

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ABSTRACT: *A Mathematical Model was developed for the spread and control of Lassa Lever. Existence and stability were analysed for disease free equilibrium. Key to our analysis is the basic reproductive number* (R_0), *which is an important threshold for disease control. Reasonable sets of values for the parameter in the model were compiled, and sensitivity analysis indices of* R_0 *around the baseline parameter value were computed, which shows that the most sensitive parameter to* R_0 *is human birth rate* β_H, *followed by condom efficacy and compliance. Further, the numerical computation of* R_0 *gave a value of 0.129, finally, numerical simulations were obtained that illustrates the effects of the control parameters on the various compartments of the model.*

KEYWORDS: Stability, Sensitivity, Endemic, Lassa fever, Equilibrium, spectral radius,

INTRODUCTION

Lassa fever is an acute viral Hemorrhagic fever (VHF) first isolated in a town called Lassa in the Yedseram River Valley in the present Borno State of Northern Nigeria in 1969 (Tara, 2004). Lassa fever is endemic in Nigeria, Liberia, Sierra Leone, Guinea, and other West African countries, affecting about 2 – 3 million persons with 5000 - 10,000 fatalities annually (McCormick, et al 1987). Since its initial discovery in Lassa-Nigeria, rural and nosocomial outbreaks of Lassa fever have occurred repeatedly in other parts of Nigeria: Jos, Onitsha, Zonkwa, Ekpoma (Tomori, et al, 1988).

Promed (2006) reported outbreaks in some cities of West African countries of Sierra Leone, Liberia, Guinea. In Côte d'Ivoire, Ghana, Togo and Benin, no outbreak has ever been recorded, though isolated cases show evidence of viral circulation (Gunther et al, 2001). Lassa fever therefore appears to have 2 geographically separate endemic areas: the Mano River region (Guinea, Sierra Leone, and Liberia) in the West, and Nigeria in the East. However, Some Lassa fever cases have been "imported" into the U.S. and U.K. through travelers who acquired the disease elsewhere (Tara, 2004).

Lassa fever is a zoonotic disease, i.e. it can be transmitted from infected animal to a human. The natural Reservoir of the Lassa virus is Multimammate Rat species known as Mastomys Natalencesis (Fisher-Hoch et al, 1995). Because certain varieties of *Mastomys* often live in human homes, the virus is easily transmitted to humans. Transmission occurs via direct contact with rat urine, faces, and saliva; via contact with excretion- or secretion-infected materials; or via ingestion of excretion-contaminated food. Victims can also become infected via skin breaks, and via mucous membranes from aerosol transmission from dust-borne particles. In some areas, the rodents are used as a food source, thus providing additional exposure to the infected rat blood, as well as allowing ingestion of potentially contaminated meat. Eze et al,

(2010) stated that Health workers become infected usually from contact with rodent saliva or contamination of needles.

Unlike other arena viruses, Lassa virus can be fairly easily transmitted from human to human the (WHO, 2004). Richmond (2000) stated that humans can contact the disease from other humans via aerosol transmission (coughing), or from direct contact with infected human blood, urine, or semen. Lassa virus has been isolated from semen 6 weeks after acute illness; thus the virus can be transmitted to sexual partners by convalescent men (Tara, 2004).

The symptoms of Lassa fever develop about 21 days after the infection with acute illness involving multi organs. Specific symptoms include fever, facial swelling, muscle fatigue, vomiting, cough, meningitis, and hypertension. In some patients neurological problems, including hearing loss which may be transient or permanent, tremors, and encephalitis, have been described the (Omalibu et al, 2005)

LITERATURE

Okuonghae and Okuonghae (2006) formulated a SIS model coupled to a population of rat species, for the transmission of Lassa fever disease. They obtained the equilibrium states of their model and examined them for endemic and epidemic situations. Further, they calculated the basic reproductive number for their model and gave conditions for disease outbreak. Ogabi, et al (2012) developed a SIR model for controlling Lassa fever transmission in northern part of Edo state, Nigeria. They advocated for health policies that will keep the basic reproductive number R_0 below 1, thereby keeping the transmission of the disease under control.

The Lassa fever model developed by (Bawa, et al 2013) is a major shift from the first two papers cited. The researchers divided the human population into susceptible human S_H and the Infect human I_H, the reservoir population they divided into Infant I_R and the Adult reservoir A_R and interestingly represented the Virus in the environment by V they explained that the virus compartment is generated from the urine and faeces of infected Human and adult reservoirs. The major parameters of their model are b_H per capital birth rate of Human, b_R per capital birth rate of the reservoir, μ_R per capital natural death rate of Human, μ_H per capital death rate of the reservoir, δ_H Lassa fever induced death rate, δ_R mortality death of the reservoir due to hunting, β_1 effective contact rate for human, β_2 effective contact rate between reservoir and human, γ recovery rate of Infected human and σ progression rate from Infant to adult reservoir. They recommended that efforts should be made to keep the basic reproductive number below unity to ensure that the virus is contained.

Onuorah et al (2016) developed a Lassa fever model using the sex structure approach. Their model represented the transmission dynamics of the Lassa fever disease using a set of ordinary differential equations. The total human population at time t denoted by $N_H(t)$ was sub-divided into four (4) mutually exclusive sub-populations of Susceptible Male $S_1(t)$, Infected Male $I_1(t)$, Susceptible Female $S_2(t)$, Infected Female $I_2(t)$, such that $N_H(t) = S_1(t) + I_1(t) + S_2(t) + I_2(t)$. Similarly, the total Natural Reservoir/host population at time t, denoted by $N_R(t)$ was sub-divided into dormant Reservoir host $R_1(t)$, active Reservoir host $R_2(t)$, such that $N_R(t) = R_1(t) + R_2(t)$. Their model had the following assumptions.

Susceptible individuals, male/female can be infected via interaction with the active Reservoir (Mastomys Natelensis), and via sexual interaction with opposite sex. Two major controls were considered, the use of condom to reduce contact via sexual interaction and the use of pesticide/Rat poison to kill the natural Reservoir (Mastomys Natelensis). And finally, horizontal transmission for human and vertical transmission for the Reservoir.

In this paper we extended an earlier work Onuorah et al (2016), specifically, we included a schematic diagram, sensitivity analysis, numerical computation of the basic Reproductive number R_0 numerical simulation.

METHODOLOGY

Parameters of the Model

β_H The natural Birth rate of human population

β_R The natural birth rate of vectors

θ The proportion of human birth that is male $0 < \theta < 1$

ρ Spectral Radius

α_1 The rate of transmission resulting from sexual interaction between infected female and susceptible male

α_2 The rate of transmission resulting from sexual interaction between infected male and susceptible female

α_3 The rate of transmission resulting from interaction between active virus Reservoir and susceptible male

α_4 The rate of transmission resulting from interaction between active virus Reservoir and susceptible female

c_1 Average number of male partners acquired by a susceptible female

c_2 Average number of female partners acquired by a susceptible male

μ_1 Natural death rate of human population

μ_2 Natural death rate of Reservoir population

γ Recovery rate of infected human

σ Progression rate from dormant to active Reservoir host

δ_1 Death rate of human population due to infection

δ_2 Death rate of virus Reservoir population due to application of pesticide

ε Efficacy of condom

τ Compliance of condom usage

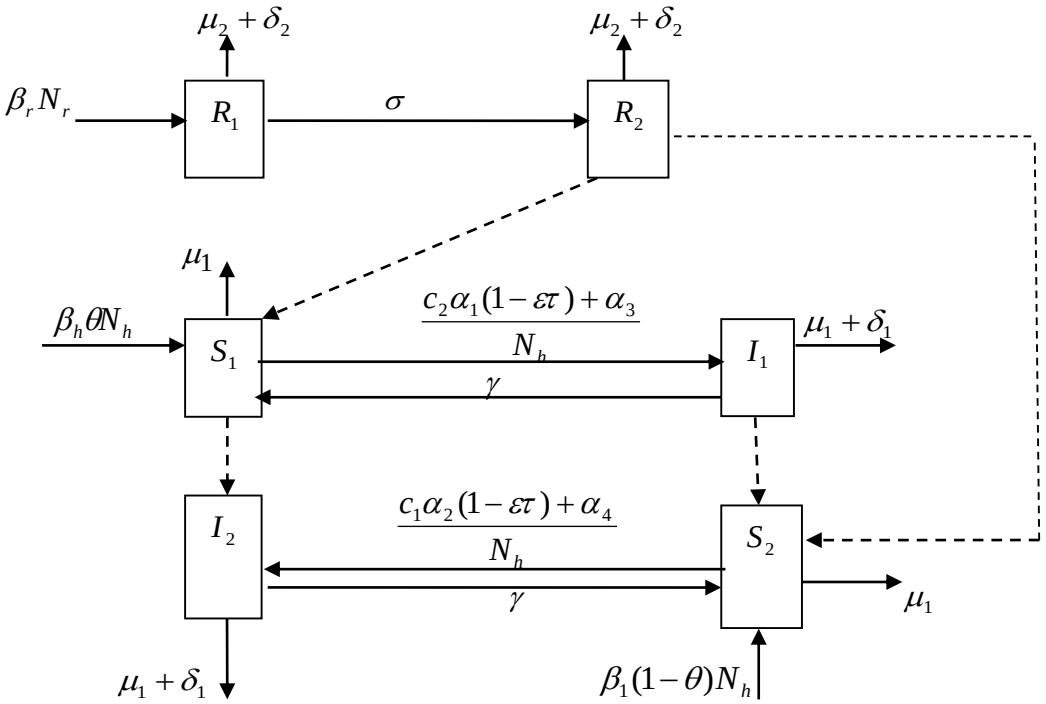

Figure 1. A schematic description of the model

Interaction ----------▶ ——————▶ Flow

Interaction here results to infection while flow indicates movement from one compartment to another as the individuals change status.

The Model

From the assumptions and the schematic diagram above we have the following equations:

$$\frac{dI_1}{dt}=\frac{(c_2\alpha_1(1-\varepsilon\tau)I_2+\alpha_3R_2)S_1}{N_H}-(\mu_1+\delta_1+\gamma)I_1 \quad (2)$$

$$\frac{dS_2}{dt}=\beta_H(1-\theta)N_H+\gamma I_2-\frac{(c_1\alpha_2(1-\varepsilon\tau)I_1+\alpha_4R_2)S_2}{N_H}-\mu_1S_2 \quad (3)$$

$$\frac{dI_2}{dt}=\frac{(c_1\alpha_2(1-\varepsilon\tau)I_1+\alpha_4R_2)S_2}{N_H}-(\mu_1+\delta_1+\gamma)I_2 \quad (4)$$

$$\frac{dR_1}{dt}=\beta_RN_R-(\sigma+\mu_2+\delta_2)R_1 \quad (5)$$

$$\frac{dR_2}{dt}=\sigma R_1-(\mu_2+\delta_2)R_2 \quad (6)$$

The total human population size is given by;

$$N_H = S_1 + I_1 + S_2 + I_2 \quad (7)$$

The total Reservoir population size is given by

$$N_R = R_1 + R_2 \quad (8)$$

By adding equations (1) to (4), we have;

$$\frac{dN_H}{dt} = \beta_H N_H - \mu_1 N_H - \delta_1 (I_1 + I_2) \quad (9)$$

By adding equations (5) to (6), we have;

$$\frac{dN_R}{dt} = \beta_R N_R - (\mu_2 + \delta_2) \quad (10)$$

Basic Properties of the Model

In this section, the basic dynamical features of the model equations (1) to (6) will be explored.

Theorem 1 The closed set

$$D = \left\{ (S_1, I_1, S_2, I_2, R_1, R_2) \in \Re_+^6 : S_1 + I_1 + S_2 + I_2 \le \frac{\beta_H}{\mu_1 N_H}; R_1 + R_2 \le \frac{\beta_R}{(\mu_2 + \delta_2)} \right\}$$

Is positively-invariant and attracting with respect to the basic model equations (1) to (6)

Proof

From equations (7), to (10);

$$\frac{dN_H}{dt} \le \beta_H - \mu_1 N_H, \ \frac{dN_R}{dt} \le \beta_R - (\mu_2 + \delta) N_R.$$

It follows that $\frac{dN_H}{dt} < 0$ and $\frac{dN_R}{dt} < 0$ if $N_H(t) > \frac{\beta_H}{\mu_1}$ and $N_R(t) > \frac{\beta_R}{\mu_2}$ respectively. Thus a standard comparison theorem as in (Lakshmickantham et al, 1999) can be used to show that $N_H(t) \le N_H(0) e^{\mu_1(t)} + \frac{\beta_H}{\mu_1}\left(1 - e^{-\mu_1(t)}\right)$ and $N_R(t) \le N_R(0) e^{\mu_2(t)} + \frac{\beta_r}{\mu_2 + \delta_2}\left(1 - e^{(-\mu_2 + \delta_2)(t)}\right)$. In particular $N_H(t) \le \frac{\beta_H}{\mu_1}$ and $N_R(t) \le \frac{\beta_R}{\mu_2 + \delta_2}$ if $N_H(0) \le \frac{\beta_H}{\mu_1}$ and $N_R(0) \le \frac{\beta_R}{\mu_2 + \delta_2}$ respectively. Thus D is positively-invariant. Further, if $N_H(0) > \frac{\beta_H}{\mu_1}$, and $N_R(0) > \frac{\beta_R}{\mu_2 + \delta_2}$, then either the solution enters D in finite time or $N_H(t)$ approaches $\frac{\beta_H}{\mu_1}$, and $N_R(t)$ approaches $\frac{\beta_R}{\mu_2 + \delta_2}$, and the infected variables $I_1 + I_2$ approaches 0. Hence D is attracting,

that is all solutions in $\Re_+^6$ eventually enters D. Thus in D, the basic model equations (1) to (6) is well posed epidemiologically and mathematically according to (Hethcote, 1978). Hence it is sufficient to study the dynamics of the basic model equations (1) to (6)

Disease Free Equilibrium (DFE)

At equilibrium states, the rate of change of the state variables with respect to time is zero, i.e.

$$\frac{dS_1}{dt}=\frac{dI_1}{dt}=\frac{dS_2}{dt}=\frac{dI_2}{dt}=\frac{dR_1}{dt}=\frac{dR_2}{dt}=0$$

We define disease compartments as the Infected male, Infected female compartments that is I_1 and I_2. we let $(S_1, I_1, S_2, I_2, R_1, R_2)=(x, y, z, u, v, w)$ at disease free equilibrium, equations the right hand side of our model equation (1) to (6) to zero and solving with the above change of variable, we have our DFE

$$E_0=(x,y,z,u,v,w)=\left(\frac{\beta_H\theta N_H}{\mu_1},0,\frac{\beta_H(1-\theta)N_H}{\mu_1},0,0,0\right) \quad (11)$$

Local **Stability of Disease Free Equilibrium** E_0

The notion of stability of equilibrium is of considerable theoretical and practical importance, and has been widely discussed in the literature (Anderson and May, 1991), (Driessche and Wathmought, 2005).

For us to analyses our disease free equilibrium for stability we first obtain the Jacobian matrix at disease free equilibrium and basic reproductive number of our model.

At DFE, the Jacobian matrix is

$$J_{E_0}=\begin{bmatrix} -\mu_1 & \gamma & 0 & \frac{px}{N_H} & 0 & \frac{\alpha_3 x}{N_H} \\ 0 & -A_1 & 0 & \frac{px}{N_H} & 0 & \frac{\alpha_3 x}{N_H} \\ 0 & \frac{qz}{N_H} & -\mu_1 & 0 & 0 & \frac{\alpha_4 z}{N_H} \\ 0 & \frac{qz}{N_H} & 0 & -A_1 & 0 & \frac{\alpha_4 z}{N_H} \\ 0 & 0 & 0 & 0 & -A_2 & 0 \\ 0 & 0 & 0 & 0 & \sigma & -(\mu_2+\delta_2) \end{bmatrix} \quad (12)$$

where $P=c_2\alpha_1(1-\varepsilon\tau)$, $q=c_1\alpha_2(1-\varepsilon\tau)$ $A_1=(\mu_1+\delta_1+\gamma)$ and $A_2=(\mu_2+\delta_1+\gamma)$

Basic Reproductive Number (R_0)

One of the most important concerns about any infectious disease is its ability to invade a population. Many epidemiological models have a disease free equilibrium (DFE) at which the population remains in the absence of the disease. These models usually have a threshold parameter, known as the basic reproductive number R_0 such that when $R_0 < 1$, then the DFE is locally asymptotically stable, and the disease cannot invade the population, but if $R_0 > 1$,then the DFE is unstable and invasion is always possible see (Hethcote,1978).

We define the basic reproductive number R_0 as the number of secondary infections that one infective individual would create over the duration of the infectious period provided that everyone else is susceptible. We use the next generation matrix approach as described by (Driessche and Wathmough, 2005) to derive our Basic Reproductive Number diseases.

Here, the basic reproductive number R_0 is the spectral radius of the product matrix

FV^{-I}, i.e. $R_0 = \rho(FV^{-I})$

Our model has two Infective compartments namely the Infective male I_1, and Infected female I_2. It follows that the matrices F and V for the new infective terms and remaining transfer terms respectively are given below:

.

$$F = \begin{bmatrix} 0 & \frac{px}{N_H} \\ \frac{qz}{N_H} & 0 \end{bmatrix} \qquad V = \begin{bmatrix} A_1 & 0 \\ 0 & A_1 \end{bmatrix}$$

$$FV^{-I} = \begin{bmatrix} 0 & \frac{px}{N_H A_1} \\ \frac{qz}{N_H A_1} & 0 \end{bmatrix}$$

(13)

The spectral radius of (30) is given by

$$\rho(FV^{-I}) = \sqrt{\frac{px.qz}{(N_H A_1)^2}}$$

Substituting the values of x, z at equilibrium, the values of A_1, p and q gives

$$R_0 = \sqrt{\frac{(c_2\alpha_1(1-\varepsilon\tau)\beta_H\theta)\times(c_1\alpha_2(1-\varepsilon\tau)\beta_H(1-\theta))}{\mu_1((\mu_1+\delta_1+\gamma))^2}} \qquad (14)$$

THEOREM 2: The disease free equilibrium of the model equations (1) to (6) is locally asymptotically stable (LAS) if $0 < R_0 < 1$

Proof

Though the local stability of DFE when $R_0 < 1$ is a direct consequence of theorem 2 in (Driessche and Wathmough, 2005) which need not be proved, however we confirm the correctness of the theorem by using the standard linearization technique. We transform (12) presented above to an upper triangular matrix using elementary row reduction method to have;

$$J_{E_0} = \begin{bmatrix} -\mu_1 & \gamma & 0 & \frac{px}{N_H} & 0 & \frac{\alpha_3 x}{N_H} \\ 0 & -A_1 & 0 & \frac{px}{N_H} & 0 & \frac{\alpha_3 x}{N_H} \\ 0 & 0 & -\mu_1 & 0 & 0 & A_4 \\ 0 & 0 & 0 & -A_1 + A_3 & 0 & A_4 \\ 0 & 0 & 0 & 0 & -A_{2\nu} & 0 \\ 0 & 0 & 0 & 0 & \sigma & -(\mu_2 + \delta_2) \end{bmatrix} \quad (15)$$

where

$$A_3 = \frac{qzpx}{A_1 (N_H)^2} + \gamma, A_4 = \frac{qzpx}{A_1 (N_H)^2}\gamma + \frac{\alpha_3}{N_H},$$

Thus the characteristics equation of the upper triangular Jacobian matrix (15) is given by;

$$J_{E_0} = \begin{bmatrix} -(\mu_1 + \lambda) & \gamma & 0 & \frac{px}{N_H} & 0 & \frac{\alpha_3 x}{N_H} \\ 0 & -(A_1 + \lambda) & 0 & \frac{px}{N_H} & 0 & \frac{\alpha_3 x}{N_H} \\ 0 & 0 & -(\mu_1 + \lambda) & 0 & 0 & A_4 \\ 0 & 0 & 0 & -(A_1 - A_3 + \lambda) & 0 & A_4 \\ 0 & 0 & 0 & 0 & -(A_2 + \lambda) & 0 \\ 0 & 0 & 0 & 0 & \sigma & -(\mu_2 + \delta_2 + \lambda) \end{bmatrix} \quad (16)$$

Equating the product of the diagonal of an upper triangular Jacobian matrix to zero gives the Eigen-values of the matrix, therefore the Eigen values of (16) are;

$$\lambda_1 = \lambda_3 = -\mu_1, \lambda_2 = -A_1, \ \lambda_4 = -(\mu_1 + \delta_1 + \gamma) + \frac{qzpx}{(N_H)^2(\mu_1 + \delta_1 + \gamma)}, \ \lambda_5 = -A_2, \ \lambda_6 = (\mu_2 + \delta_2)$$

For local stability of disease free equilibrium Routh-Hurwitz criteria requires that all Eigen values have negative real part. Since all the Eigen-values of (16) are negative, i.e.

$\lambda_i < 0$ for $i = 1,2,3..6$ implies $R_1 < 1$, hence the disease free equilibrium DFE is locally asymptotically stable if $R_1 < 1$

Global Stability of Disease Free Equilibrium

Global stability of epidemiological model is necessary and makes the model predictable as it guarantees that the model is independent of the initial size of the population. Global asymptotic stability (GAS) of an epidemiological model can be established by constructing appropriate Lyapunov function (Garba and Gumel, 2010). However, to establish the GAS of our model, we adapt the method used in (Castilo- Chavez et al 2002), see appendix C.

THEOREM 3. The disease free equilibrium of the model equations (1) to (6) is Globally Asymptotically stable (GAS) if $R_0 < 1$.

Proof

To establish the global stability of the disease free equilibrium, the two conditions (H1) and (H2) as in Castilo- Chavez et al 2002) must be satisfied for $R_0 < 1$. We write the model equations (1) to (6) in the form

$$\frac{dX_1}{dt} = F(X_1, X_2)$$

$$\frac{dX_2}{dt} = G(X_1, X_2); G(X_1, 0)$$

where $X_1 = (x, z, v, w)$ and $X_2 = (y, u)$

With the components of $X_1 \varepsilon R^4$, denoting uninfected population and the components of $X_2 \varepsilon R^2$ denoting the infected population.

From (11)

$$E_0 = (X_1^*, 0), X_1^* = \left(\frac{\beta_H \theta N_H}{\mu_1}, 0, \frac{\beta_{hH}(1-\theta) N_H}{\mu_1}, 0, 0, 0 \right) \quad (17)$$

Now for the first component, that is globally asymptotically stability of X_1^*, we have

$$\frac{dX_1}{dt} = F(X_1, 0) = \begin{bmatrix} \beta_H \theta N_H - \mu_1 x \\ \beta_H (1-\theta) N_H - \mu_1 z \\ 0 \\ 0 \end{bmatrix} \quad (18)$$

From equation (18) we solve the first equation i.e.

$$\frac{dx}{dt} = \beta_R \theta N_H - \mu_1 x$$

Using integrating factor (IF)

we have

$$\frac{dx}{dt} + \mu_1 x = \beta_R \theta N_H \tag{19}$$

Which give our IF as

$$IF = e^{\int \mu_1 dt} = e^{\mu_1 t} \tag{20}$$

Multiplying both sides of (19) by our IF, we have

$$e^{\mu_1 t}\frac{dx}{dt} + e^{\mu_1 t}\mu_1 x = e^{\mu_1 t}\beta_R \theta N_H \tag{21}$$

Integrating both sides of (21), we have

$$e^{\mu_1 t}x + C_1 = \frac{\beta_R \theta N_H}{\mu_1} e^{\mu_1 t} + C_2 \tag{22}$$

$$e^{\mu_1 t}x = \frac{\beta_R \theta N_H}{\mu_1} e^{\mu_1 t} + C_2 - C_1 \tag{23}$$

$$e^{\mu_1 t}x = \frac{\beta_R \theta N_H}{\mu_1} e^{\mu_1 t} + C \tag{24}$$

Multiplying both sides of (24) by $e^{-\mu_1 t}$

we have

$$x(t) = \frac{\beta_R \theta N_H}{\mu_1} + Ce^{-\mu_1 t} \tag{25}$$

where

$C = C_2 - C_1$

For $x(0) = 0$

we have that

$$C = -\frac{\beta_R \theta N_H}{\mu_1}^{-\mu_1 t} \tag{26}$$

Substituting (26) above into (25), we have:

$$x(t) = \frac{\beta_H \theta N_H}{\mu_1} - \frac{\beta_H \theta N_H e^{-\mu_1 t}}{\mu_1} + x(0)e^{-\mu_1 t} \tag{27}$$

Similarly,

$$z(t) = \frac{\beta_H (1-\theta) N_H}{\mu_1} - \frac{\beta_H (1-\theta) N_H e^{-\mu_1 t}}{\mu_1} + z(0)e^{-\mu_1 t} \tag{28}$$

we have $x(t)+z(t)\to 1 \text{as } t\to\infty$

Regardless of the value of $x(0)$, and $z(0)$

Thus $X_1^* = \left(\frac{\beta_H \theta N_H}{\mu_1}, 0, \frac{\beta_{hH}(1-\theta)N_H}{\mu_1}, 0,0,0\right)$ is globally asymptotically stable.

Next for the 2nd condition, that is

$G(X_1, X_2) = AX_2 - G(X_1, X_2)$, we have that

$$A = \begin{bmatrix} -(\mu_1+\delta_1+\gamma) & \frac{px}{N_H} \\ \frac{qz}{N_H} & -(\mu_1+\delta_1+\gamma) \end{bmatrix} \quad (29)$$

This is clearly an M-matrix (the off diagonal elements of A are non-negative

$$G(X_1, X_2) = \begin{bmatrix} \frac{(pu+\alpha_3 w)x}{N_H} & -(\mu_1+\delta_1+\gamma) \\ \frac{(qy+\alpha_4 w)z}{N_H} & -(\mu_1+\delta_1+\gamma) \end{bmatrix} \quad (30)$$

then,

$\hat{G}(X_1, X_2) = AX_2 - G(X_1, X_2) \geq 0 =$

i.e.

$\hat{G}(X_1, X_2) \geq 0$

Since all the parameters are assumed to be non-negative, it is obvious that

$\hat{G}(X_1, X_2) \geq 0$, and this completes the proof.

RESULTS

Baseline Parameter Values

Lassa fever has 2 geographically separate endemic areas: the Mano River region (Guinea, Sierra Leone, and Liberia) in the West, and Nigeria in the East, (Gunther, 2004). We show baseline values Table 1 for parameters of our model. For human population in our model, we consider villages, and small towns within Edo state where there is high transmission in Nigeria.

Table 1. Baseline Parameter values for the model equations (1) to (6)

Parameter	Values	References
β_H	0.038	CIA (2015)
β_R	0.56	Estimate
θ	0.6	Estimate
α_1	0.6	Estimate
α_2	0.5	Estimate
α_3	0.6	Estimate
α_4	0.6	Estimate
c_1	2	Williams et al (1996)
c_2	3	Williams et al (1996)
μ_1	0.02	CIA (2015)
μ_2	0.6	Estimate
γ	0.9	Estimate
σ	0.8	Estimate
δ_1	0.2	Estimate
δ_2	0.3	Estimate
ε	0.8	Garba and Gumel (2010)
τ	0 – 1	Abdulrahaman (2014).

Sensitivity Analysis

Sensitivity tells us how important each parameter is to disease transmission. Such information, is crucial not only to experimental design, but also to data assimilation and reduction of complex nonlinear model (Poweell, 2005). Sensitivity Analysis is commonly used to determine the robustness of model prediction to parameter values, since there are usually errors in data collection and presumed parameter values. It is used to determine parameters that have high impact on the R_0 and should be targeted by intervention strategies.

Sensitivity indices allows us to measure the relative changes in a variable when a parameter changes. The normalised forward sensitivity index of a variable with respect to a parameter is the ratio of relative changes in the parameter when the variable is a differentiable function of the parameter. The sensitivity index may be alternatively defined using partial derivatives. The normalised forward sensitivity index of R_0 that depends differentially on a parameter p is defined by

$$\Gamma_P^{R_0} = \frac{\partial R_0}{\partial P} \times \frac{P}{R_0} \qquad (31)$$

Given the explicit formula for R_0 one can easily derive an analytical expression for the sensitivity of R_0 with respect to each parameter that comprise it. The obtained values are given in table 2. Below which present the sensitivity index for the base line parameter values in table1. Above, the index table reveals that the most sensitive parameter to our Basic

Reproductive number is β_H. For example, $\Gamma_{c_1}^{R_0} = +0.5$ means that increasing (or decreasing) c_1 of by 10% increases (or decrease R_0 by 5%. The maple code that generated our sensitivity index is Appendix B

Table 2. Sensitivity indices of the basic Reproductive number R_0

	Parameter	*Sign*	*Value*
1	β_H	+	***1***
2	ε	–	***0.92307***
3	τ	–	***0.92307***
4	δ_1	+	***0.9***
5	μ_1	–	***0.517850.4999***
6	c_1	+	***0.5***
7	α_2	+	***0.5***
	α_1	+	***0.49999***
9	c_2	+	***0.499990***
10	γ	–	***0.1785***
11	θ		***0***

Numerical Simulation

In this section, we use the Maple 13 software to plot the graph of the numerical solution of our model equations. The initial condition for each plot is stated, the parameters values are as given in table 4.4 above. Figures 4.1 to 4.6 are numerical simulation of the Lassa Fever model given by equations (1) to (6), using the original system variables with parameter values as given in table 1. The simulations were conducted using the Runge-Kuta method (rkf45) embedded in Maple 13. The rkf45 method is a fourth-order method, meaning that the local truncation error is on the order of $0(h^5)$, while the total accumulated error is order $0(h^4)$.

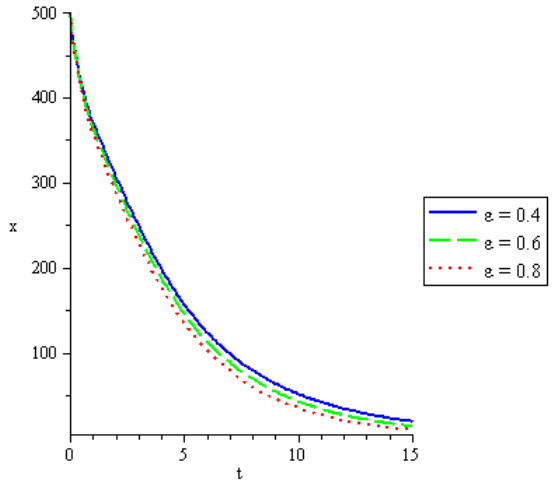

Figure 1. The graph of Infected female population x(t) against time t, with initaial condition 500, varrying values of condon efficacy (ε) other paramter values are as shown in table 1.

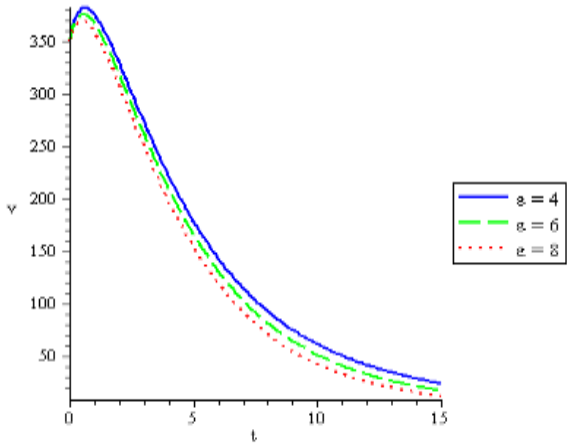

Figure 2. The graph of Infected Male population v(t) against time t, with initaial condition 350, varrying values of condom efficacy (ε) other paramter values are as shown in table 1.

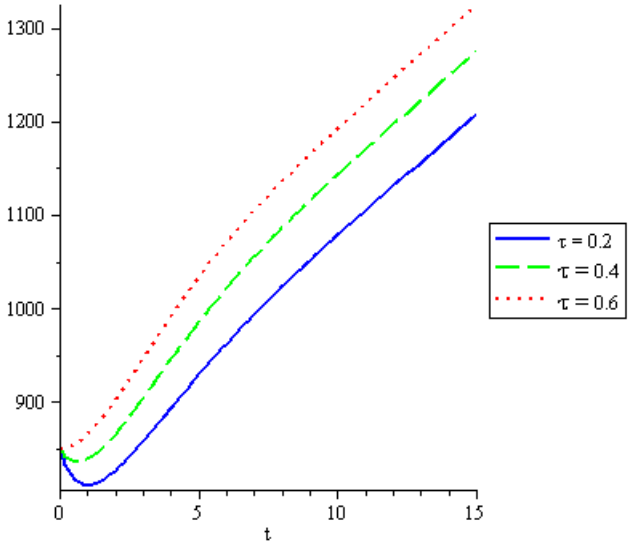

Figure 4. The grapg of Suceptible Male population u(t) against time t, with initial condtion 850,varrying values of τ, other parameter values are as given in table 1.

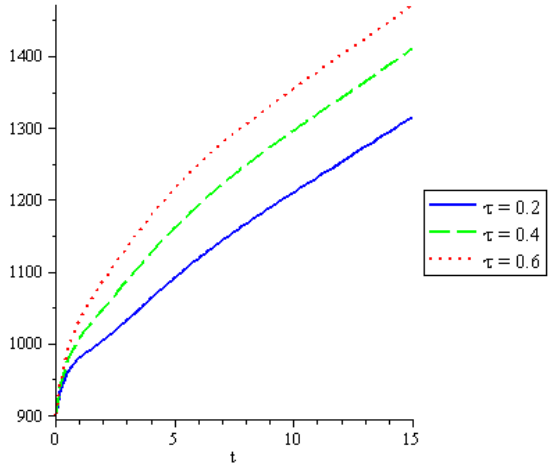

Figure 3. The grapg of Suceptible female population w(t) against time t, with initial condtion 900,varrying values of condom compliance (τ) other parameter values are as given in table 1.

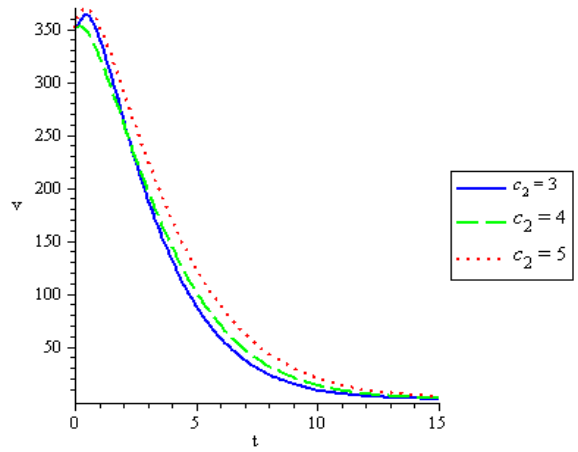

Figure 5. The graph of Infected Male v(t) against time, t with initail condition 350, varrying values of female sexual partner c_2, *other paramters values are as* **in** *table* 1.

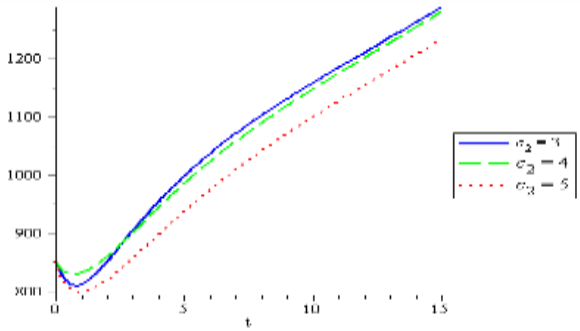

Figure 6. The graph of Susceptible male, u(t) against time, t with initail condition 850, varrying values of female sexual partner c_2, *other paramters values are as* **in** *table* 1.

CONCLUSION

The sensitivity analysis shows that the most sensitive parameter to the basic reproductive number R_0 is the human birth rate, followed by the condom efficacy and compliance. The

A Mathematical Model with standard incidence is developed and analysed to study the transmission and control of Lassa Fever. Mathematically we modelled Lassa Fever as a six – dimensional system of non – linear ordinary differential equation. We first show that there exist a domain D where our model is Mathematically and Epidemiologically well posed The Model incorporates two control parameters, condom efficacy (ε) and compliance (τ) and δ_2 which is the rate at which both the dormant and active vector are killed due to the use of Rodenticide/Rat poison. The Disease Free Equilibrium point of the model was obtained, and analysed for stability. We obtained an important threshold parameter Basic Reproductive

Number R_0, it is known that when $R_0 \leq 1$ the disease dies out, and when $R_0 > 1$ the disease persists in the population.

Because we are interested in control, we carried out a sensitivity analysis of the basic Reproductive number, which shows that the most sensitive parameter to the basic reproductive number R_0 is the birth rate of human β_H, followed by condom efficacy (ε) and compliance (τ). The analysis and numerical simulation shows the effects of the control parameters on the various compartments of the model. For instance figure1 is a simulation of the effects of condom efficacy ε on the Infected Female population $v(t)$. It shows that for all the values of τ the population decreases directly with time. The higher the values of ε the faster the population approaches zero and the lower the values of ε the more time it takes the Infected population to approach zero.

FURTHER RESEARCH

The basic reproductive number computed (0.129) is low, yet the virus is fast spreading in Nigeria and some other countries of the world. This informed further study on the endemic equilibrium and Bifurcation analysis which will indicate that reducing R_0 is not enough to ensure that the virus will be contained.

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APPENDIX A

Computation of Basic Reproductive Number R_0

```
> restart

> with(Basic Reproductive number, R0)

with(Basic Reproductive number, R0)

> β[H] := 0.038; θ := 0.5; α[1] := 0.9; α[2] := 0.8; c[1] := 2; c[2]
      := 3; μ[1] := 0.02; ι := 0.9; δ[1] := 0.2; ε := 0.8; τ := 0.6
```

$\beta_H := 0.038$

$\theta := 0.5$

$\alpha_1 := 0.9$

$\alpha_2 := 0.8$

$c_1 := 2$

$c_2 := 3$

$\mu_1 := 0.02$

$\iota := 0.9$

$\delta_1 := 0.2$

$\varepsilon := 0.8$

$\tau := 0.6$

```
> R0
      := (((c[2]·α[1]·(1 − ε·τ)·β[H]·θ)·(c[1]·α[2]
      ·(1 − ε·τ)·β[H]·(1 − θ)))^(1/2))/(μ[1]·(ι + μ[1] + δ[1])·(ι
      + μ[1] + δ[1]))
```

$R_0 := 0.1296479925$

APPENDIX B

Sensitivity Indices of the Basic Reproductive Number R_0

```
> restart
> with(Sensitivity Analysis of R0 wrt birth rate of Human, βH)
```

with(Sensitivity Analysis of^2 R_0 wrt birth rate Human, β_H)

```
> θ := 0.5; α[1] := 0.9; α[2] := 0.8; c[1] := 2; c[2] := 3; μ[1]
    := 0.02; ι := 0.9; δ[1] := 0.2; ε := 0.8; τ := 0.6
```

$\theta := 0.5$

$\alpha_1 := 0.9$

$\alpha_2 := 0.8$

$c_1 := 2$

$c_2 := 3$

$\mu_1 := 0.02$

$\iota := 0.9$

$\delta_1 := 0.2$

$\varepsilon := 0.8$

$\tau := 0.6$

```
> R0
    := (((c[2]·α[1]·(1 − ε·τ)·β[H]·θ)·(c[1]·α[2]
    ·(1 − ε·τ)·β[H]·(1 − θ)))^(1/2))/(μ[1]·(ι + μ[1] + δ[1])·(ι
    + μ[1] + δ[1]))
```

$R_0 := 3.411789284\sqrt{\beta_H^2}$

```
> k := diff(R0, βH)
```

$k := \frac{3.411789284\beta_H}{\sqrt{\beta_H^2}}$

```
> βH := 0.038
```

$\beta_H := 0.038$

> $\Upsilon[\beta[H]] := \frac{k \cdot \beta_H}{R_0}$

$Y_{0.038} := 1.000000000$

> *restart*

> $with\left(Sensitivity\ Analysis\ of\ \ R_0 wrt\ probaility\ of\ male\ birth, \theta\right)$

$with\left(Sensitivity\ Analysis\ of^2\ R_0\ wrt\ probaility\ male\ birth, \theta\right)$

> $\beta_H := 0.038; \alpha[1] := 0.9; \alpha[2] := 0.8; c[1] := 2; c[2] := 3; \mu[1] := 0.02; \iota := 0.9; \delta[1] := 0.3; \varepsilon := 0.8; \tau := 0.6$

$\beta_H := 0.038$

$\alpha_1 := 0.9$

$\alpha_2 := 0.8$

$c_1 := 2$

$c_2 := 3$

$\mu_1 := 0.02$

$\iota := 0.9$

$\delta_1 := 0.3$

$\varepsilon := 0.8$

$\tau := 0.6$

> $R_0 := (((c[2] \cdot \alpha[1] \cdot (1 - \varepsilon \cdot \tau) \cdot \beta[H] \cdot \theta) \cdot (c[1] \cdot \alpha[2] \cdot (1 - \varepsilon \cdot \tau) \cdot \beta[H] \cdot (1 - \theta))) / (\mu[1] \cdot (\iota + \mu[1] + \delta[1]) \cdot (\iota + \mu[1] + \delta[1])))^{1/2}$

$R_0 := 0.2380422163\sqrt{\theta\ (1 - \theta)}$

> $k := diff\left(R_0, \theta\right)$

$k := \frac{0.1190211082(1 - 2\,\theta)}{\sqrt{\theta\ (1 - \theta)}}$

> $\theta := 0.5$

$\theta := 0.5$

> $\Upsilon[\theta] := \frac{k \cdot \theta}{R_0}$

$Y_{0.5} := 0.$